Remarks

Claims 7-11 and 15-22 are pending in the subject application. By this Amendment, the applicants have amended claims 7, 11, 17 and 22. Support for the claim amendments can be found in the specification as originally filed including at page 1, lines 11-14 and page 9, line 35 to page 10, line 12. No new matter has been added by these amendments. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 7-11, 15-22 are currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

The amendments set forth herein have been made in an effort to lend greater clarity to the claimed subject matter and to expedite prosecution. These amendments should not be taken to indicate the applicants' agreement with, or acquiescence to, the rejections of record. Favorable consideration of the claims now presented, in view of the remarks and amendments set forth herein, is earnestly solicited.

Initially, the applicants wish to note that the reference (cite No. R8) that was submitted to the Patent Office in an Information Disclosure Statement on October 24, 2005 was not initialed as having been considered by the Examiner. Attached herewith is a copy of Form PTO Form 1449 for the Examiner's review. The applicants' kindly request that the Examiner initial the reference as being considered by the Examiner and please return a copy of form to the undersigned.

Claims 17, 18 and 21 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement, more particularly for failing to enable "prevention." Although the applicants do not agree with this rejection, in order to expedite prosecution the claims have been amended herein to delete the term "preventing," thereby, rendering moot this ground for rejection.

Claims 7-10, 15-19 and 21 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Bijlsma *et al.* (US Patent No. 6,686,341 and WO 00/57727). The applicants respectfully traverse this ground for rejection.

The Office Action states that "the polysaccharides disclosed by Bijlsma *et al.* can have as many as 1 in 10 or 1 in 3 saccharide units modified with a phosphate group. Since polysaccharides of over 10 kD will have [more] than about 500 saccharide units per polymer, …substantially all of

them will have at least one phosphate group" (Office Action, page 11). Therefore, the Examiner concludes that the polysaccharides disclosed by Bijlsma *et al.* meet "the requirements of [the] limitation that at least 90% of the molecules of dextran be phosphorylated" (Office Action, page 12).

By this amendment the applicants have amended claims 7 and 17 to clarify that "at least 90% of the hydroxyl groups in the dextran molecules are phosphorylated." Since Bijlsma *et al.* describe nutritional compositions which contain only "slightly" negatively charged polysaccharides and expressly teach away from polysaccharides that contain "too many negatively charged groups" (U.S. Patent , columns 5-8; WO Pub., pages 7-12), Bijlsma *et al.* do not disclose or suggest the method now claimed. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §103 based on Bijlsma *et al.*

Claim 22 has been rejected under 35 U.SC. §103(a) as being unpatentable over Bijlsma *et al.* as applied to claims 7-10, 15-19 and 21 above, and further in view of Tarelli *et al.* (Anal Biochem 222:196-201, 1994). The applicants respectfully traverse this ground for rejection because the cited references, either taken alone or in combination, do not disclose or suggest the applicants' method as now claimed.

The Office Action states that Tarelli *et al.* disclose a method of phosphorylating saccharides and other OH-containing compounds wherein the polysaccharide is dissolved in a phosphate buffer, freeze-dried, and heated to 56C for a period of days" (Office Action, page 13). Accordingly, the Office Action concludes that "[i]t would have been obvious to one of ordinary skill in the art at the time of the invention to make a phosphorylated dextran for use in the invention of Bijlsma *et al.*, using the freeze-drying and 24 hour heating steps as described by Tarelli *et al.*" (Office Action, page 13).

To expedite prosecution, the applicants have amended claim 22. Specifically, the phosphorylated dextran has now been defined as having a molecular weight of at least 100,000 and immunopotentiating activity, wherein at least 90% of the hydroxyl groups in the dextran molecules are phosphorylated. Furthermore, step (d) which recites "confirming that at least 90% of the hydroxyl groups in the dextran molecules are phosphorylated" has been introduced.

It is well established in the patent law that the mere fact that the purported prior art could have been modified or applied in some manner to yield an applicant's invention does not make the modification or application obvious unless "there was an apparent reason to combine the known elements in the fashion claimed" by the applicant. *KSR International Co. v. Teleflex Inc.*, 550 U.S. ____ (2007). Furthermore, an applicant's invention is not "proved obvious merely by demonstrating that each of its elements was, independently, known in the (purported) prior art." *Id.* In this case, the applicants respectfully submit that there is no reason to modify the cited references to arrive at the current invention and, thus, there is no *prima facia* case of obviousness.

Since the Bijlsma *et al.* reference expressly teaches away from a high degree of phosphorylation, and Tarelli *et al.* fail to disclose or suggest a phosphorylated dextran in which at least 90% of the hydroxyl groups are phosphorylated, one of ordinary skill in the art would have had no reason to confirm that at least 90% of the hydroxyl groups in the dextran molecules are phosphorylated. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §103 based on Bijlsma *et al.* in view of Tarelli *et al.*

Claims 11 and 20 have been rejected under 35 U.SC. §103(a) as being unpatentable over Bijlsma *et al.* as applied to claims 7-10, 15-19 and 21 above, and further in view of Suzuki *et al.* (Carbohydrate Res 53:223-229, 1977) in view of Sacco *et al.* (Carbohydrate Res 184:193-202, 1988). The applicants respectfully traverse this ground for rejection because the cited references, either taken alone or in combination, do not disclose or suggest the current invention.

The Office Action states that "Suzuki *et al.* discloses a phosphorylated dextran and a method of making said dextran phosphate by reacting the dextran with polyphosphoric acid and trichylamine in anhydrous formamide. ...Sacco *et al.* discloses a method of phosphorylating dextran comprising heating dextran in the presence of tributylamine and polyphosphoric acid" (Office Action, page 14). Accordingly, the Office Action asserts that "[i]t would have been obvious to one of ordinary skill in the art at the time of the invention to make dextran phosphates of Bijlsma *et al.* by the reaction of Suzuki *et al.* carried out under heating" (Office Action, page 14).

The applicants have also amended claim 11 to clarify that "at least 90% of the hydroxyl groups in the dextran molecules are phosphorylated." Moreover, an additional step which recites "confirming that at least 90% of the hydroxyl groups in the dextran molecules are phosphorylated" has been introduced.

The shortcomings of the primary Bijlsma *et al.* reference with respect to the current invention have been discussed above. The Suzuki *et al.* reference and the Sacco *et al.* reference do not cure, or even address, these shortcomings.

Specifically, the cited references, either taken alone or in combination, do not disclose or suggest a phosphorylated dextran in which at least 90% of the hydroxyl groups are phosphorylated. Therefore, it would not have been obvious to one of ordinary skill in the art at the time of the instant invention to confirm that at least 90% of the hydroxyl groups in the dextran molecules are phosphorylated. Therefore, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §103 based on Bijlsma *et al.*, Suzuki *et al.* and Sacco *et al.*

In view of the foregoing remarks and the amendments to the claims, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

The applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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DRS/la
Attachment: Copy of Form PTO-1449 submitted to the Patent Office on October 24, 2005

PTO/SB/08B (08-03)
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Substitute for form 1449B/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Complete if Known	
Application Number	10/522,047
Filing Date	January 19, 2005
First Named Inventor	Tadao Saito
Group Art Unit	
Examiner Name	
Attorney Docket Number	SPO-120

Sheet 2 of 2

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article, (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
/ESO/	R1	BABA, M. *et al.* "Mechanism of Inhibitory Effect of Dextran Sulfate and Heparin on Replication of Human Immunodeficiency Virus *In Vitro*" *Proc. Natl. Acad. Sci. U.S.A.*, August 1988, pp. 6132-6136, Vol. 85, No. 16.	
/ESO/	R2	KITAZAWA, H. *et al.* "Augmentation of Macrophage Functions by an Extracellular Phosphopolysaccharide from *Lactobacillus Delbrueckii* ssp. *Bulgaricus*" *Food Microbiology*, 2000, pp. 109-118, Vol. 17, No. 1.	
/ESO/	R3	KITAZAWA, H. *et al.* "Phosphate Group Requirement for Mitogenic Activation of Lymphocytes by an Extracellular Phosphopolysaccharide fom *Lactobacillus Delbrueckii* ssp. *Bulgaricus*" *International Journal of Food Microbiology*, 1998, pp. 169-175, Vol. 40, No. 3.	
/ESO/	R4	SUZUKI, M. *et al.* "Preparation and Antitumor Activity of O-Palmitoyldextran Phosphates, O-Palmitoyldextrans, and Dextran Phosphate" *Carbohydrate Research*, 1977, pp. 223-229, Vol. 53, No. 2.	
/ESO/	R5	TARELLI, E. *et al.* "Drying from Phosphate-Buffered Solutions Can Result in the Phosphorylation of Primary and Secondary Alcohol Groups of Saccharides, Hydroxylated Amino Acids, Proteins, and Glycoproteins" *Analytical Biochemistry*, 1994, pp. 196-201, Vol. 222, No. 1.	
/ESO/	R6	UEMURA, J. *et al.* "Chemical Characterization of Exocellular Polysaccharide from *Lactobacillus Delbrueckii* subsp. *Bulgaricus* OLL1073R-1" *Milchwissenschaft*, 1998, pp.443-446, Vol. 53, No. 8.	
/ESO/	R7	NISHIMURA-UEMURA, J. *et al.* "Functional Alteration of Murine Macrophages Stimulated with Extracellular Polysaccharides from *Lactobacillus Delbrueckii* ssp. *Bulgaricus* OLL1073R-1" *Food Microbiology*, 2003, pp. 267-273, Vol. 20.	
	R8	WHISTLER, R. L. *et al.* "Preparation and Characterization of Polysaccharide Phosphates" *Archives of Biochemistry and Biophysics*, 1969, pp. 396-401, Vol. 135, No. 1.	
	R9		
	R10		
	R11		
	R12		
	R13		

Examiner Signature	/Eric Olson/	Date Considered	09/14/2007

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] Applicant's unique citation designation number (optional). [2] Applicant is to place a check mark here if English language Translation is attached.